

### **REMARKS**

Reconsideration of the rejections set forth in the Office action mailed September 26, 2005 is respectfully requested. Claims 1, 3-4, 6-7 and 15-16 are currently pending.

#### **I. Amendments**

Claim 1 is amended to state that the "amplicon" is a cloning vector, as recited in dependent claim 2, which is accordingly cancelled.

Claim 15 has been amended to recite that the words in the oligonucleotide tags are constructed from three of the four natural nucleotides, an embodiment described in the specification at page 7, lines 30-31. Claim 16 has been amended, for clarity, to recite that "each" word is of the length range recited.

No new matter is added by any of the amendments.

#### **II. Rejections under 35 U.S.C. §112, Second Paragraph**

The pending claims 1-4 and 6-7 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to the terms "amplicon" and "opened amplicon" (Office Action, pages 203, items 4-6), the independent claim has been amended to state that the tag precursors are in a cloning vector, for consistency with the claim terms "opened amplicon" and the like.

The Examiner suggests that claim 1 states that "an 'oligonucleotide' (single stranded) and 'a duplex' (double stranded) both consist of a word" (Office Action, page 3, item 7). However, the claim does not refer to a duplex consisting of a word. Rather, the claim refers to "a duplex consisting of a word of the set *and the complement of any other word of the set*".

In view of the above, the applicants submit that the claims are in accordance with the requirements of 35 U.S.C. §112, second paragraph.

#### **III. Rejections under 35 U.S.C. §101 and 35 U.S.C. §112, First Paragraph**

The pending claims were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and use the invention without undue experimentation.

The Examiner suggests that the specification does not teach the skilled artisan how to use the claimed invention, how to synthesize "only useful oligonucleotide tags", or how to "recognize useful over non-useful oligonucleotides or vectors". In view of the citation of case law (*Genentech v. Novo Nordisk A/S*, 42 USPQ2d 1001) on page 5 of the Office Action, the Examiner alleges that the applicants have not disclosed "any specific starting material or any of the conditions under which a process can be carried out".

The pending claims were also rejected under 35 U.S.C. §101 as lacking a specific and substantial asserted utility or a well-established utility. Because the §101 requirement is related to the "how to use" requirement of §112, these issues are addressed together.

As stated in the Field of the Invention, the collections, or repertoires, of oligonucleotide tags provided by the invention are used "for identifying, sorting, and/or tracking molecules, especially polynucleotides" (page 1, lines 8-9 of specification).

This use, which was known in the art, is described more generally in the Background of the Invention, with particular reference to the "'solid phase' cloning technique described in Brenner", which employs oligonucleotide tags synthesized from sets of minimally cross-hybridizing subunits or "words". The use of such oligonucleotide tags is described further in the definition of a "word" at page 4, line 30, where the Brenner reference noted above, as well as further US patent documents, are incorporated by reference. These references provide algorithms for generating the minimally cross-hybridizing sets of words, as noted at page 8, lines 4-6. Exemplary minimally cross-hybridizing sets of words are also provided at pages 7-8 of the specification. The skilled person would thus know how to select "useful" oligonucleotides for carrying out the invention.

Accordingly, the sets of words or "tag precursors" used as "starting material" for the improved synthesis of the invention were known in the art and are exemplified in the specification. The minimally cross-hybridizing properties of these words, and the tags constructed of them, were also known in the art and are described in the specification.

The case law citation on page 5 of the Office Action also provides that "the specification...must supply the *novel* aspects of an invention" (emphasis added). It is well established in case law that the specification need not teach, however, what is well known in

the art. (A patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics Inc. v. Coherent Inc.* 827 F.2d 1524, 3 USPQ2d 1737, CAFC 1987; *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 231 USPQ 81, CAFC 1986. A patent need not disclose what is well known in the art. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1331, CAFC 1991. The skilled worker need only be able to locate the information relied on for enablement with no more than reasonable diligence. *In re Howarth* 654 F.2d 103, 210 USPQ 689, CCPA 1981.)

In the present application, one "novel aspect" of the invention relates to improved methods of synthesizing oligonucleotide tags and their complements, to reduce synthesis errors and thus improve sorting fidelity. See, for example, the specification at page 2, line 31 to page 3, line 21. The synthetic processes are described in detail at page 10, line 33 and following, and a person having general knowledge in the field regarding oligonucleotide synthesis, restriction enzymes, ligation, cloning, amplification, etc., would easily have been able to carry out the claimed processes. The accuracy of the synthetic processes can also be verified by sequencing, as demonstrated at page 24, line 23 and following.

A further novel aspect relates to the tag repertoires (claims 15-16) prepared by the claimed processes, in that these tags have one or more nucleotides intervening between "words". As noted in the specification at, for example, page 16, lines 15-18, these tag repertoires can be used in a manner similar to the tag repertoires of the prior art.

In view of the above, the applicants submit that the claims are in accordance with the requirements of 35 U.S.C. §101 and 35 U.S.C. §112, second paragraph.

#### IV. Rejections under 35 U.S.C. §102(b)

Claims 15-16 were rejected under 35 U.S.C. §102(b) as being anticipated by GIBCO BRL Products and Reference Guide, pages 17-19. As stated by the Examiner, this publication discloses random primers which are described as "truly random" and "mostly hexamers". Thus, one could conclude that a set of all possible hexamers is disclosed.

However, the oligonucleotide tags in the claimed repertoires have a minimum length of 13 nucleotides. That is, in the formula  $w_1(N)_{x1}w_2(N)_{x2} \dots (N)_{xn-1}w_n$ , each word has a minimum length of three nucleotides ("each of  $w_1$  through  $w_n$  is a word consisting of an

oligonucleotide having a length from three to fourteen nucleotides"), the tag contains at least four words ("n is an integer in the range of from 4 to 10"), and there must be at least one nucleotide intervening between adjacent words at some location in the tag ("each of  $x_1$  through  $x_{n-1}$  is an integer selected from the group consisting of 0, 1, and 2, provided that at least one of  $x_1$  through  $x_{n-1}$  is 1 or 2"). These oligonucleotide tags are therefore not anticipated by the composition of "mostly hexamers" in the cited reference.

Accordingly, the applicants request that the rejection under 35 U.S.C. §102(b) be withdrawn.

V. Conclusion

In view of the foregoing, the applicants submit that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

Respectfully submitted,



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